REMARKS

The Applicants acknowledge the Office Action of November 16, 2004 with appreciation. Claims 22-24 and 26-39 are pending in the application.

The Applicants acknowledge the Examiner's telephone interview of September 22, 2004, to discuss the Applicant's request for withdrawal of the finality of the Office Action dated April 7, 2004. In the Response After Final of July 27, 2004, the Applicants discuss the basis for questioning the prematureness of the final rejection, according to the MPEP § 706.07 (c), and also petition under 37 CFR § 1.181 for the withdrawal of the finality with the Response. Agreement was not reached.

The Applicants discussed the basis to question the prematureness of the Final Rejection with Primary Examiner, Rodney P. SWARTZ, Ph.D. in a telephone interview of October 5, 2004. The Applicants conferred that the Office improperly made the Action final in view of a newly cited basis for rejection in the Office Action. Agreement was not reached.

The Applicants discuss the basis for questioning the finality of the Office Action in telephone interviews with Supervisory Patent Examiner, Lynette F. SMITH on October 5, 2004 and October 7, 2004. Supervisor SMITH considered the Applicant's position regarding the prematureness of the finality of the Action. Primary Examiner SMITH agreed that the Final Rejection was improperly imposed and vacated the Final Rejection and Advisory Action.

The Office has withdrawn rejections of claims 22-24 and 26-39 under 35 U.S.C. § 103 as being obvious over Haeuw, et al. A certified English translation of the French Priority was provided to the Office March 8, 2004, thereby perfecting the convention priority claim. The submission of the priority document removes Haeuw, et al. as prior art and obviates the rejection.

The Office rejects Claims 22-24 and 26-39 under 35 U.S.C. § 103(a) as being obvious over Rauly, et al., (Research in Immunology 1998, Vol. 149:99) in view of Cooper, et al., (Journal of Infectious Diseases, 1983, 147:312-317). The Office construes that Rauly, et al. teach a *Klebsiella pneumoniae* OmpA combined with an antigen or hapten but do not teach intranasal administration and that Cooper, et al. teach intranasal administration of *Klebsiella pneumoniae*. The Office concludes that it would be *prima facie* obvious to administer the immunogen of Rauly, et al. through intranasal administration as taught by Cooper, et al. to arrive at the instant method for improving immunity.

To further distinguish the instant invention the Applicants, hereby, amend generic Claim 22 to include language which clarifies that the instant method is drawn to improving systemic immunity and also to include language to clarify that the instant method of improving systemic immunity is through intranasal administration of an immunologically effective amount of the pharmaceutical composition.

The Applicants submit that the teaching of Rauly, et al. and Cooper, et al. do not make obvious the instant method of improving systemic immunity of a mammal with respect to an antigen or a hapten, through intranasal administration of an immunologically effective amount of a pharmaceutical composition comprising, the *Klebsiella pneumoniae* membrane protein OmpA having the sequence SEQ ID No. 2, combined with the antigen or the hapten. In support of this assertion, the Applicants submit the following.

Rauly, et al. disclose the use of a recombinant *Klebsiella pneumoniae* OmpA, P40 coupled with a B-cell epitope. Cooper, et al. teach intranasal immunization with inactivated *Klebsiella pneumoniae* bacteria for the development of local immunity to *Klebsiella pneumoniae* in the lower respiratory tract (see Title and Abstract). The subject matter of Cooper, et al. pertains to the development of local immunity to a mucosal pathogen by intranasal administration, which is not the instant method for enhancing systemic immunity with respect to an antigen or hapten.

Cooper, et al. evaluate the protective immunity against the respiratory pathogen following intranasal immunization with *Klebsiella pneumoniae*. Cooper, et al. discuss immunity upon intranasal administration stating, "It is clear that the levels of serum antibody could not be correlated with the level of immunity expressed by these animals. In particular, low levels of serum antibodies were found in the group immunized intranasally (table 1)." (Results section, page 314). Cooper, et al. teach that the local protection following intranasal immunization is attributed to immunoglobulins found in the lung secretions from mice immunized intranasally (Table 2). Therefore, Cooper, et al. teach intranasal administration of inactivated *Klebsiella pneumoniae* for local immunity to this respiratory pathogen.

With regard to systemic immunity, Cooper, et al. teach intravenous immunization to improve systemic immunity and demonstrate a correlation between immunity and serum antibody levels which was established by the two intravenous immunized groups, where a fourfold difference in HA activity correlated with a similar difference in LD_{50} as determined by the method of Reed and Muench (page 314). Cooper, et al. recite, "Immunity to intranasal infection is produced by systemic immunization resulting in high titers of circulating antibody." (see Abstract). Cooper, et al. quantitate the level of serum antibodies generated by either intranasal or intravenous administration of the immunogen (Table 1, HA units/ml). Based on these results, Cooper, et al. demonstrate that a systemic antibody response is achieved through intravenous administration of *Klebsiella pneumoniae*. Thus, Cooper, et al. teach improving systemic immunity through systemic immunization and teach away from the instant method of improving systemic immunity through intranasal administration. Therefore, based on the teaching of Cooper, et al., the Applicants submit that one skilled in the art would not be inclined to administer a *Klebsiella pneumoniae* membrane protein OmpA combined with an antigen or hapten to improve systemic immunity through intranasal administration and, consequently, there is no motivation to combine the teaching of Rauly, et al. with the teaching of Cooper, et al.

The instant method of improving systemic immunity, as evidenced by the increased antibody levels in the serum following intranasal administration of a *Klebsiella*

pneumoniae OmpA combined with an antigen or hapten, is demonstrated in Examples 5 and 6 of the instant Specification. The demonstrated serum antibody levels elicited by the instant method distinguishes from Cooper, et al. which disclose that no antibody could be detected by HA in the serum of mice immunized intranasally (page 314, Results section, fourth paragraph). In view of the foregoing, the Applicants submit that the teaching of Rauly, et al. and Cooper, et al. do not make obvious the instant method for improving systemic immunity of a mammal with respect to an antigen or a hapten, through intranasal administration of a pharmaceutical composition comprising the *Klebsiella pneumoniae* OmpA.

In view of the instant amendment, drawn to improving systemic immunity, the Applicants submit that the Office has not established a *prima facie* case of obviousness. Reconsideration and withdrawal of the prior art rejection is respectfully solicited.

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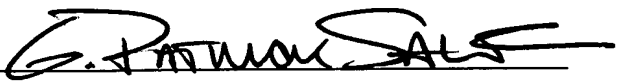
Accordingly, entry of the present amendment, reconsideration of all grounds of objection and rejection, withdrawal thereof, and passage of this application to issue are all hereby respectfully solicited.

It should be apparent that the undersigned attorney has made an earnest effort to place this application into condition for immediate allowance. If he can be of assistance to the Examiner in the elimination of any possibly-outstanding insignificant impediment to an immediate allowance, the Examiner is respectfully invited to call him at his below-listed number for such purpose.

Allowance is solicited.

Respectfully submitted,
THE FIRM OF HUESCHEN AND SAGE

By: 

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Enclosure: Listing of Claims; Extension Fee, two (2) months, check in the amount of $450.00 and Postal Card Receipt

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THE COMMISSIONER IS HEREBY AUTHORIZED TO CHARGE ANY FURTHER OR ADDITIONAL FEES WHICH MAY BE REQUIRED (DUE TO OMISSION, DEFICIENCY, OR OTHERWISE), OR TO CREDIT ANY OVERPAYMENT, TO DEPOSIT ACCOUNT NO. 08,3220.